REMARKS

Any fees that may be due in connection with the filing of this paper or with this application may be charged to Deposit Account No. 06-1050. If a Petition for Extension of time is needed, this paper is to be considered such Petition.

The attached substitute listing of claims replaces the listing of claims filed with the Amendment After Final on December 12, 2005. In claim 1 of the claim listing filed on December 12, 2005, status identifiers in several claims inadvertently were not updated. Accordingly the status identifier of claim 1 has been corrected to properly reflect that claim 1 was previously presented and no further amendments to claim 1 are presented. Similarly, the status identifiers of claims 35, 100, 101, and 102 have been corrected. In addition, the amendments to the claims filed on December 12, 2005, are resubmitted herewith. No further amendments to the claims have been made.

Claims 1-23, 25-37, 49-54, 93-95, 99-102 are pending in this application Claims 1, 11 17, 18, 21-23, 34 and 35 are amended Claim 11, 25, 26 and 99 are amended to correct the inadvertent word processing error in which subscripts printed incorrectly.

Applicant is requesting reconsideration because it respectfully is submitted that it appears that the Examiner has failed to consider a significant element of all of the claims: that the combination contain:

a) a collection of capture agents that specifically bind to preselected polypeptides; and

b) a collection of oligonucleotides that encode the preselected polypeptides to which the capture agents specifically bind.

The Examiner has not pointed or noted any teaching in any reference of record that teaches, suggests or discloses these requisite elements. The Examiner states that the oligonucleotides in the collections of Dower *et al.* can encode polypeptides, but does not show (nor would it be possible to show) that Dower *et al.* discloses, teaches or suggests that such polypeptides are preselected polypeptides which capture agents in a first collection are designed to bind. There are additional distinctions between the disclosures and teachings of the cited references and the instant claims; such distinctions were previously addressed. This response focuses on this important distinction that appears to have been overlooked by the Examiner. Therefore, it is requested that the Examiner acknowledge and consider this limitation that is in the pending and in the original claims.

It respectfully is submitted that the instant claims are clearly novel and unobvious over the cited references. The undersigned respectfully requests that the Examiner call her to discuss this application, if this distinction is not clear. The discussion in the previous response is repeated below and additions are included. Also, the comments in the Advisory Action are discussed at the end of this paper.

THE CLAIMS

Independent claim 1 is directed to a combination that contains two collections. The first collection is a collection of capture agents in which each capture agent specifically binds to a preselected polypeptide. The second collection contains oligonucleotides that **encode the preselected polypeptides to which the capture agents bind.**

The capture compound collection contains at least M members; and the oligonucleotide collection contains at least "m" members. Each E_m is unique in the oligonucleotide collection. The collection of oligonucleotides encodes at least 10 different preselected polypeptides The collection of capture agents contains at least 10 sets of capture agents, where each set is specific for a different preselected polypeptide Em. Dependent claims specify particulars regarding the combinations.

The claims are *not* directed to complexes formed between the oligonucleotides and the capture agents. The combination contain *two collections*. ***Significantly every claim requires that the oligonucleotides encode polypeptides to which the capture agents specifically bind.*** It respectfully is submitted the Examiner has ignored this significant requirement.

THE REJECTIONS UNDER 35 U.S.C. §102(b)

Claims 1-9,11-23, 25-36, 93 and 100 are rejected under 35 U.S.C. §102(b) as being anticipated by Lerner *et al.* This rejection is respectfully traversed for the reasons of record and the arguments set forth herein.

Differences between the disclosure of Lerner *et al.* and the instant claims

Lerner *et al.* discloses combinatorial libraries in which each member of the library is tagged with a nucleic acid molecule that by *virtue of its sequence identifies* the library member to which it is linked. This is achieved by parallel synthesis of the library member and the nucleic acid in which each nucleotide is a code for a particular chemical unit in the library member. This library of oligonucleotide-tagged compounds is screened with "preselected biological molecules of interest." Molecules from the library that bind are

identified by virtue of their tag. The combinatorial libraries disclosed by Lerner et al. bear no resemblance to the instantly claimed combinations nor to member collections..

The oligonucleotide tags disclosed by Lerner *et al.* **do not encode** the preselected biological molecules nor do they encode preselected polypeptides to which the compounds bind. The indexers do not encode polypeptides; they may represent a code but they are not translatable into a polypeptide. Furthermore, the libraries of Lerner *et al.* include small molecules; clearly an oligonucleotides indexer that is a code for that to which it is linked, is different from an oligonucleotides the encodes a polypeptide. There is a difference between something that is a code for something else and an oligonucleotides that encodes something.

Claims are read in light of the specification; it is clear upon reading the instant specification, the oligonucleotides, when translated, encode polypeptides. For example, as described in the specification, the oligonucleotides are linked to members of nucleic acid libraries, and are then translated to produce polypeptide libraries that are captured by the capture agents. The methods in which the combinations are used are sorting methods in which the oligonucleotides, linked to DNA encoding polypeptides, are translated. The translated products are reacted with the capture agents, and the polypeptides encoded by the oligonucleotides bind to the capture agents. These are methods of sorting to reduce diversity.

The polypeptides encoded by the oligonucleotides specifically bind to the capture agents. As described by Lerner *et al.* the library members, not their linked oligonucleotides indexer, bind to the capture agents. So even if Lerner *et al.* disclosed indexers that encoded polypeptides, the capture agents used by Lerner *et al.* bind to library members, not to the oligonucleotides nor to polypeptides encoded thereby. These are methods in which capture agents select members of the library.

Analysis

As noted above and in the previous response, the products disclosed in Lerner *et al.* differ from the instantly claimed combinations in a variety of elements. Lerner *et al.* does not disclose a combination of two collections: a collection of capture agents and a collection of oligonucleotides where the members of the collection of capture agents that bind to preselected polypeptides and the collection of oligonucleotides ***encode the preselected polypeptides to which the capture agents bind.*** There is a one-to-one correspondence; the collection of oligonucleotides encodes (literally) upon translation, the polypeptides to which the capture agents bind.

The oligonucleotides of Lerner *et al.* provide codes that identify the members of the combinatorial library to which each is linked; each oligonucleotide **does not** encode the polypeptides to which compounds in the library bind. The oligonucleotides are linked to the library members; they do not encode polypeptides to which the "preselected biological molecules of interest" bind.

The Examiner states that the oligonucleotide identifier defines the structure of the chemical polymer. In the instant claims, the oligonucleotides **do not** define the structure of a chemical polymer nor of the capture compounds, but **encode the polypeptides** to which the capture compounds bind. The Examiner urges that the oligonucleotides of Lerner *et al.* encode polypeptides and points to a codon. This is **not the same** as encoding the preselected polypeptides to which the capture agents bind, which is an element of all of the presently pending claims.

Since anticipation requires that a reference disclose every element of a claim, Lerner *et al.*, which does not disclose a combination containing a collection of capture agents and a collection of oligonucleotides that encodes the polypeptides to which the captures agents bind, does not anticipate any of the rejected claims nor any of the presently pending claims.

Claims 1, 2, 11, 12, 25, 26, 36, 49-51, 99 and 101

Claims 1, 2, 11, 12, 25, 26, 36, 49-51, 99 and 101 are rejected under 35 U.S.C. §102(b) as being anticipated by Dower *et al.* (U.S. Patent No. 5,639,603) because Dower *et al.* discloses synthetic chemical libraries, which the Examiner urges correspond to the oligonucleotides of the instant claims, and binding reaction complexes. The Examiner states that the encoded synthetic libraries "comprise beads, identifier tags, and oligomers" and that the identifier tags are oligonucleotides that include "monomer specific information/coding site." This rejection is respectfully traversed.

Differences between the disclosure of Dower *et al.* and the instant claims

Dower *et al.* discloses methods for tagging the products of combinatorial chemical syntheses to produce encoded synthetic libraries. The combinatorial products are tagged with identifiers that are distinguishable. The identifier tags are used to track the synthesis of the members of the combinatorial library and serve to identify the member to which each is linked. The identifier tag can be an oligonucleotide in which the sequence identifies the reaction steps (*i.e.*, each base, or sequence thereof, indicates that a particular reaction was

employed), and hence the resulting molecule. The oligonucleotide tags, as with Lerner *et al.*, are used to encode information regarding the structure of the linked combinatorial library member. The oligonucleotides *do not* encode preselected polypeptides to which capture agents in a second collection bind. Capture agents in the method are used to screen the combinatorial library members, not something encoded by the tag. Dower *et al.* does not disclose a combination that contains two collections: (a) a collection of capture compounds that bind to preselected polypeptides; and (b) **a collection of oligonucleotides that encode the preselected polypeptides.**

Analysis

As noted, Dower *et al.* fails to disclose a combination that contains two collections: (a) a collection of capture compounds that bind to preselected polypeptides; and (b) a collection of oligonucleotides that encode the preselected polypeptides. Further, if the oligonucleotides of Dower *et al.* correspond to the oligonucleotides in the instant claims as urged by the Examiner, then they differ from oligonucleotides of the instant claims because they are encoded with information regarding sequence steps that produced the library member to which each is bound; they do not encode polypeptides to which a collection capture agents (which the Examiner urges are the capture agents used to screen the combinatorial library) bind. The so-called capture agents as disclosed in Dower *et al.* bind to combinatorial library members, not to polypeptides that are encoded by the oligonucleotides linked to the combinatorial library members. In the instant claims, the capture agents are specific for polypeptides encoded by the oligonucleotides, not for members of a combinatorial library that are linked to the oligonucleotides. Therefore, because Dower *et al.* fails to disclose numerous elements of the instant claims, it does not anticipate any of the instant claims.

In the Final Office Action, the Examiner describes the methods and collections of Dower, but does not identify where Dower discloses a combination of two collections in which a first collection contains capture agents that bind to preselected polypeptides, and the second collection contains oligonucleotides that **encode the preselected polypeptides to which the capture agents in the first collection bind**. It respectfully is submitted that the Examiner has ignored this element of the instant claims. This element is not disclosed or suggested by Dower *et al.* nor any reference of record.

THE REJECTION OF CLAIMS 1-9, 11-23, 25-36, 49-54 AND 93-95 UNDER 35 U.S.C. §103(a)

Relevant Law

In order to set forth a prima facie case of obviousness under 35 U.S.C. § 103: (1) there must be some teaching, suggestion or incentive supporting the combination of cited references to produce the claimed invention (ACS Hospital Systems, Inc. v. Montefiore Hospital, 732 F.2d 1572, 1577, 221 USPQ 329, 933 (Fed. Cir. 1984)) and (2) the combination of the cited references must actually teach or suggest the claimed invention. Further, that which is within the capabilities of one skilled in the art is not synonymous with that which is obvious. Ex parte Gerlach, 212 USPQ 471 (Bd. APP. 1980). Obviousness is tested by "what the combined teachings of the references would have suggested to those of ordinary skill in the art." In re Keller, 642 F.2d 413, 425, 208 USPQ 871, 881 (CCPA 1981), but it cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching or suggestion supporting the combination (ACS Hosp. Systems, Inc. v Montefiore Hosp. 732 F.2d 1572, 1577. 221 USPQ 329, 933 (Fed. Cir. 1984)). "To imbue one of ordinary skill in the art with knowledge of the invention in suit, when no prior art reference or references of record convey or suggest that knowledge, is to fall victim to the insidious effect of a hindsight syndrome wherein that which only the inventor taught is used against its teacher" W.L. Gore & Associates, Inc. v. Garlock Inc., 721 F.2d 1540, 1553, 220 USPQ 303, 312-13 (Fed. Cir. 1983). The mere fact that prior art may be modified to produce the claimed product does not make the modification obvious unless the prior art suggests the desirability of the modification. In re Fritch, 23 U.S.P.Q.2d 1780 (Fed. Cir. 1992); see, also, In re Papesch, 315 F.2d 381, 137 U.S.P.Q. 43 (CCPA 1963).

Claims 1-9, 11-23, 25-36, 49-51 and 93-95

Claims 1-9, 11-23, 25-36, 49-51 and 93-95 are rejected under 35 U.S.C. §103(a) as being unpatentable over Lerner *et al.* and Dower *et al.* for reasons of record. This rejection is respectfully traversed.

The claims

The claims are discussed above and in the previous response

The cited references

The teachings of each of Lerner *et al.* and Dower *et al.* are discussed above and in the previous response.

Analysis

The Examiner has failed to set forth a *prima facie* case of obviousness because the combination of teachings of the cited references does not result in the instantly claimed combinations and systems. The combination of teachings of Lerner *et al.* with those of Dower *et al.* does not result in the instantly claimed combinations and systems. As discussed above, neither Lerner *et al.* nor Dower *et al.* teaches or suggests a combination that contains two collections where one collection is a collection of capture agents that bind to preselected polypeptides and the other is a collection of oligonucleotides **that encode the polypeptides to which the capture agents bind**. Each of Lerner *et al.* and Dower *et al.* teaches oligonucleotide-tagged combinatorial libraries in which the sequence of the oligonucleotide provides information regarding the structure of library member to which it is linked, and any "capture agents" (the preselected molecules for screening a library) are used to screen the combinatorial library.

The instant claims **require** that members of the collection of capture agents specifically **bind to the polypeptides encoded by the collection of oligonucleotides**. The oligonucleotides described in either or both of the cited references do not encode the encode the library members nor do they encode any polypeptides to which the "capture agents" bind. There is no teaching or suggestion in either reference to modify the oligonucleotides so that they encode polypeptides to which capture agents binds. The capture agents are used to screen the library members, not polypeptides encoded by the oligonucleotides. Neither reference, singly or in combination, teaches a combination that contains two collections as instantly claimed. Thus, the teachings of combined teachings of Lerner *et al.* and Dower *et al.* are deficient in failing to teach these requisite elements, as well as others, of the instant claims. Therefore, the Examiner has failed to set forth a *prima facie* case of obviousness.

As with the rejections for anticipation, the Examiner has not addressed the element of the claims that require the oligonucleotides to encode the polypeptides to which the capture agents bind. None of the references of record disclose, teach or suggest such combination of two collections in which one collection, a collection of capture agents, specifically binds to preselected polypeptides, that are encoded by the second collection of oligonucleotides.

Claims 1-9, 11-23, 25-36, 49-54 and 93-95

Claims 1-9, 11-23, 25-36, 49-54 and 93-95 are rejected under 35 U.S.C. §103(a) as being unpatentable over Lerner *et al.* and Iris *et al.* (U.S. Patent No. 6,403,309) for reasons of

record because Lerner *et al.* teaches a combinatorial library that contains compositions that include a chemical polymer and an identifier oligonucleotide that defines the structure of the chemical polymer, and the binding complexes. The identifier oligonucleotide includes a "coding region" that **identifies** the structure of the linked chemical polymer. The oligonucleotide tagged combinatorial library member chemical polymers are screened by binding to biologically active molecules, such as antibodies, which can be affixed to a solid support. The Examiner urges that the only difference between the teachings of Lerner *et al.* and the instant claims is that Lerner *et al.* fails to teach a computer system with software for analyzing the results of sorting. The Examiner urges that Iris *et al.* teaches an array of antibody that capture oligonucleotide probes labelled with peptide tags and also teaches a solid phase surface that comprises a plurality of loci. Each locus contains an antibody to one or more of the peptides of the peptide labelled oligonucleotide probes. The antibodies of the array specifically bind to the peptides. Further, it is alleged that the oligonucleotide probes may be first hybridized to target DNA before being captured by the addressable antibody arrays. The Examiner urges that Iris *et al.* also teaches an array that includes a computer system so that it would have been obvious to one of ordinary skill in the art to have included a computer system in the products of Lerner *et al.* . This rejection is respectfully traversed for reasons of record and those set forth below.

CLAIMS

See above

ANALYSIS

Differences between the teachings of the cited references and the instant claims

Lerner *et al.*

Lerner *et al.* is discussed above. As noted, the oligonucleotides taught by Lerner *et al.* do not encode the linked polymer, nor does Lerner *et al.* teach combinations that contain *two* collections: a collection of capture molecules that specifically bind to preselected polypeptides (they are not *specifically bound to preselected polypeptides)*; and a second collection, **a collection of oligonucleotides that encode the preselected polypeptides.**

Iris *et al*,

Iris *et al.* does not cure the deficiencies in the teachings of Lerner e*et al.* Iris *et al.* teaches polypeptide labels used in nucleic acid screening, such as for genotype mapping and gene expression analysis. The polypeptides taught by Iris *et al.* are chemically linked to

oligonucleotides; the oligonucleotides do *not* encoded the linked polypetides. The oligonucleotides hybridize with nucleic acid molecules in solution. Antibody arrays bind to the peptide-olionucleotide-nucleic acid molecule complexes. The oligonucleotides *do not* encode polypeptides to which the antibody arrays bind.

The claims

As noted above, claim 1 and claims dependent thereon are directed to combinations that contain at least two collections: a collection of capture agents that bind to preselected polypeptides, and a collection of oligonucleotides that encode the preselected polypeptides to which the capture agents bind.

Analysis

As discussed above, Lerner *et al.* fails to teach a combination of two collections, fails to **teach oligonucleotides that encode the preselected polypeptides to which the capture agents** specifically bind, and fails to teach other elements of claim 1 and all dependent claims. Iris *et al.* does not cure these deficiencies. Iris *et al.* teaches arrays of antibodies and oligonucleotide probes. Iris *et al.* does not teach oligonucleotides that encode polypeptides to which the capture agents bind. First, the oligonucleotides described by Iris *et al.* are hybridization probes that hybridize with other nucleic acid molecules (column 7, line 65-column 8, line 2). Second, the oligonucleotides do not encode polypeptides to which the antibodies of the array bind. The oligonucleotides are chemically attached to peptide tags and *it is the peptide tags* to which the antibodies bind; **the oligonucleotides do not encode the peptides tags.** Third, Iris *et al.* does not teach any oligonucleotides that encode the peptide tags. Thus, Iris *et al.* does not teach any oligonucleotides that *encode* a polypeptide to which the antibodies bind. Therefore, Iris *et al.* does not teach any elements that Lerner *et al.* fails to teach.

The Office Actions have urged that column 21, lines 29-39 of Iris *et al.* describes peptide tags that are specific for the antibodies of the array. This paragraph states only that "[t]he peptide label is used as an affinity label for binding to chip-based antibody arrays" and then cites a number of references for methods of attaching peptide labels to oligonucleotides. Notwithstanding this, Iris *et al.* does not teach that the oligonucleotides encode the polypeptides to which the antibodies bind.. As noted above, the peptide tags disclosed by *Iris et al.* are chemically attached to the oligonucleotide probes, they are not encoded by the oligonucleotide probes. .

Therefore the combination of teaching teachings of Lerner *et al.* and Iris *et al.*, does not result in the instantly claimed combinations and systems for reasons of record, including the fact that **neither reference teaches or suggests a collection of capture agents that bind to preselected polypeptides and collection of oligonucleotides that encode the preselected polypeptides.** Thus, the Examiner has failed to set forth a *prima facie* case of obviousness.

The Examiner urges that the oligonucleotides of Lerner *et al.* or Dower *et al.* encode polypeptides. While not conceding that this is correct, even if it is, neither Lerner *et al.* nor Dower *et al.* teaches or suggests that the oligonucleotides encode preselected polypeptides to which capture agents bind. Therefore, the instantly claimed combinations and systems cannot be anticipated nor rendered obvious by any combination of cited references of record.

Claims 101 and 102 are rejected under 35 U.S.C. §103(a) as being unpatentable over Dower *et al.* and Furka *et al.* (also apparently referred to in the rejection as Cheung *et al.*) because Dower *et al.* allegedly teaches all elements of these claims except for linkage to colored beads and Furka *et al.* (Cheung *et al.*) allegedly teaches microspheres that include fluorescent dyes. This rejection is respectfully traversed.

As discussed above, all claims, including claims 101 and 102, require that the claimed combinations include two collections: the first a collection of capture agents that bind to preselected polypeptides; and the second a collection of oligonucleotides **that encode the preselected polypeptides to which the capture agents bind**. As discussed above, neither Dower *et al.* nor any reference of record, including Furka *et al.* teaches or suggests such combination of elements. Therefore, the Examiner has failed to set forth a *prima facie* case of obviousness.

* * *

Advisory Action

In the Advisory Action, the Examiner urges that the collection of oligonucleotides encode the preselected polypeptides to which the capture agents bind. Each base in the oligonucleotides corresponds to one unit in the chemical polymer to which it binds. This The Examiner points out that in Figure 2, the amino acid glycine (GLY) has a corresponding oligonucleotides unit CACATG and the amino acid methionine (MET) has a corresponding unit of nucleotide sequence ACGGTA. CACATG is the codon for HIS and ATG is the codon for Met, hence CACATG does not encode GLY, but encodes HIS-MET; ACGGTA encodes THR-VAL; it does not encode MET. Lerner states that a typical and exemplary

unit identifier is based on a hexanucleotide per chemical unit. Hence the indexer does not rely on the genetic code, hence, does not **encode**, a linked polypeptide. The oligonucleotides that are linked to members of the combinatorial libraries of Lerner *et al.* do not encode the polypeptides to which they are linked and certainly do not encode preselected polypeptides to which the capture agents bind. The oligonucleotides are indexers that can be decoded to identify the linked polypeptide; they do not encode the polypeptides. Furthermore, the capture agents of Lerner *et al.* **do not bind to polypeptides encoded by the oligonucleotides;** they bind to members of the library. As pointed out by the Examiner, the exemplified indexers can employ encode polypeptides. These polypeptides, however, are not the polypeptides in the library (see, *e.g.*, Figure 2, the oligonucleotides indexer for gly-gly-gly **encodes the polypeptide HIS-MET-HIS-MET-HIS-MET), and certainly are not preselected polypeptides to which the capture agents bind. The capture agents in Lerner *et al.* bind to library members, not to polypeptides encoded by an indexer oligonucleotide.**

As discussed above, the oligonucleotides encode polypeptides, they are not codes for something, but they encode polypeptides. Claims must be read in light of the specification. One of ordinary skill in this art in reading the claims that recited that an oligonucleotides encodes a polypeptide, would understand that this means the oligonucleotides contains codons for each amino acid in a polypeptide, so that when translated (*i.e.* when used as a template for expression of proteins), a polypeptide is produced. This is an application in the field of molecular biology and proteomics. One of ordinary skill in the art would recognize that the word "encode" in this context means the genetic code. It does not mean to encrypt or to be a code for something. Lerner *et al.* **does not** describe its indexer as encoding a polypeptide to which it is linked; as exemplified the indexer clearly does not encode the amino acids to which it is linked but is a code for the molecule to which it is linked.

Again, the Examiner is invited to call the undersigned to discuss this further. It respectfully is submitted that the cited references do not teach or suggest the instantly claimed combinations. To go one Appeal on these issues would be a waste of the Applicant's very limited financial resources, and the resources of the Patent Office, including those of the Board of Appeals.

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In view of the above, consideration of the amendments and remarks herein and allowance of the application are respectfully requested.

Respectfully submitted,

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